NEW ANTIBIOTICS FROM STREPTOMYCETES

BY

BENJAMIN ELMER GREENWELL

B.S., Monmouth College, 1945

M.S., University of Illinois, 1948

AN ABSTRACT OF A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN
CHEMISTRY IN THE GRADUATE COLLEGE OF
THE UNIVERSITY OF ILLINOIS,
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INTRODUCTION

The discovery that streptomycin could be used as a valuable adjunct in the treatment of tuberculosis in man led a number of investigators in antibiotic research to concentrate their efforts on those cultures possessing antitubercular activity. Two streptomycetes, 41-31 and 21-5, isolated by Dr. David Gottlieb in the Horticulture Field laboratory of the University of Illinois, were found to possess this qualification. It was the purpose of this investigation to isolate and characterize the antibiotic substances produced by these organisms.

DISCUSSION OF RESULTS

Preliminary studies revealed that antibiotic 41-31 could be isolated from the culture media by extraction with butanol and adsorption onto carbon or Superfiltrol, but not by the use of ion-exchange resins.

Butanol extracts of the acidified media yielded a dark-brown solid residue, which could be further purified with acetone extraction. Fractionation of the active acetone-insoluble residue with methanol gave a highly active, insoluble substance. The variable results obtained with this procedure led to the investigation of another method of isolation.

Adsorption of the active principle onto Darco G-60, elution with alkaline aqueous acetone, and extraction of the eluate with diacetone alcohol yielded a diacetone alcohol-insoluble residue of low activity and a diacetone alcohol-soluble solid of high activity. The soluble fraction represented from 18 to 30 percent recovery from the culture media. Chromatography of the diacetone alcohol-soluble material over Florisil yielded a highly active, light-colored solid which contained nitrogen, displayed absorption peaks in the ultraviolet at 236, 265, and 370 mγ, and seemed to be the sodium salt of a phenolic substance. Carbon dioxide treatment of the slightly alkaline aqueous solution of this substance caused the precipitation of a very active, light-yellow solid which seemed to be the free phenol.

Antibiotic 21-5 was removed from the culture media by extraction with ether. Acetone extraction of the ether-extract residue yielded an active, waxy substance, which could be further purified by fractionation with hexane. The highly-active, hexane-insoluble residue yielded a very active tan solid, when extracted with ether. This material inhibited *M. tuberculosis* in a dilution of 1 to 150,000, but was toxic, and lacked prophylactic properties in mice.

SUMMARY

A method has been developed for the isolation of the new antibiotic produced by streptomycete 41-31. This method involved adsorption onto carbon, elution with alkaline aqueous acetone, extraction with diacetone alcohol, chromatography over Florisil, and acid precipitation of the free phenol.

The new antibiotic produced by streptomycete 21-5 was isolated by ether extraction of the culture media followed by acetone extraction, hexane extraction, and ether extraction. The highly active isolate lacked prophylactic properties and was toxic to mice.

VITA

The author was born in Monmouth, Illinois on April 26, 1924. He attended the public schools in Viola, Illinois, and, following graduation from Viola Community High School in May, 1941, entered Monmouth College, Monmouth, Illinois, in September, 1941. He received his Bachelor of Science degree with Cum Laude honors, from that institution in May, 1945. He served in the United States Navy from August, 1944 to June, 1946. He entered the Graduate College of the University of Illinois in February, 1947, and received his Master of Science degree from that institution in February, 1948. He held the position of Laboratory Assistant in Organic chemistry at the University of Illinois from February, 1948, until August, 1948. Since September, 1948, he has been a Research Fellow under the Upjohn Grant.

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